REMARKS

Claims 1-7 have been rewritten to more definitely set forth the invention and obviate the rejection. Support for the amendment of Claims 1-7 can be found in the Specification on page 6, line 27; page 7, lines 1-14; page 9, lines 15-27; page 10, lines 1-11; page 13, lines 23-27; page 15, lines 3-27; page 16, lines 1-16 and in Figs. 3, 5, 7 and 8. The present amendment is deemed not to introduce new matter. Claims 1-7 remain in the application.

Reconsideration is respectfully requested of the rejection of Claims 1-7 under 35 U.S.C. § 102(b) as being anticipated by Avrahami.

The Avrahami reference is not believed to be a proper reference under 35 U.S.C. § 102(b) since applicants are entitled to the benefit of their foreign Japanese application 11/45696 filed 02/24/1999. Applicants are accordingly submitting herewith a verified English translation of this Japanese application in order to perfect applicants' claim for priority. It is therefore believed that the Examiner would be justified in no longer maintaining the rejection in view of the submission of this verified English translation.

In any event, applicants respectfully submit that the claims as amended now clearly patentably distinguish from the disclosure of the Avrahami reference.

The present invention relates to a device and method used in an iontophoresis apparatus. In contrast, the method and device

disclosed in the Avrahami reference relates to a device for electroporation.

Iontophoresis as used in the present invention is a percutaneous absorption promoting system using electricity. This process is based on the principle that forces act on charged molecules such that positively charged molecules transfer from a positive electrode to a negative electrode and negative charged molecules migrate from the negative electrode, to the positive electrode in an electric field generated by the passage of an electric current. This process accelerates drug delivery through the skin barrier (Specification, page 1, lines 11-18).

In contrast, electroporation is well known in the art as a method of increasing pore size by the application of an electric field (Avrahami, Column 2, lines 6-10). The Avrahami reference discloses an improved apparatus and method for creating narrow channels through the stratum corneum of living skin by puncturing same (Column 2, lines 35-37).

In this connection, the Avrahami reference in column 3, lines 3-20, states that:

> "The term 'micro-channel' as used in the context of the present patent application and in the claims refers to a pathway generally extending from the surface of the skin through all or a significant part of the stratum corneum, through which pathway molecules can be fused. Preferably, micro-channels allow the diffusion therethrough of large

molecules at a greater rate than the same molecules would diffuse through pores generated by electroporation. It is believed that such micro-channels are formed due to local power dissipation leading to ablation of the stratum corneum when an electric field of such sufficient magnitude is applied to a small area of the skin, in contact with the electrodes, for a certain period of time. Unlike methods of electrically-promoted drug delivery known in the art, such as iontophoresis and electroporation, the present invention enables relatively large channels to be formed, through which even large molecules of the active substance can pass rapidly, without the necessity of ionizing or polarizing the molecules."

In view of the above disclosure of Avrahami it is believed that the present invention directed to a process and apparatus for iontophoresis patentably distinguishes from the process and apparatus for electroporation disclosed by Avrahami.

To more clearly distinguish from the Avrahami reference, Claims 1-7 have been amended to call for an iontophoresis device or method including a first means having a detection circuit for detecting a reactive current flowing through the transdermal or the transmucosal and/or a detection circuit for detecting the residual voltage developed in the transdermal or the transmucosal. That feature is found only in the present application and constitutes an important element or aspect of the present invention.

Moreover, the device called for in the claims herein for

iontophoresis is described in the Specification on page 6, line 27, to page 7, line 14. It is clear from this disclosure that when the iontophoresis apparatus is operated, charges are stored in the transdermal or transmucosal. This is referred to as a capacitance of the transdermal or the transmucosal. For example, when the drug reservoir and electrolyte reservoir are not in intimate contact with the transdermal, etc., the capacitance of the transdermal, etc., causes a decrease in reactive current and a decrease in charge (an element determining a time constant of the residual voltage) stored in the skin.

When this happens, for an output voltage, either the reactive current does not reach a predetermined value or the residual voltage does not reach a predetermined value. Thus, detecting the reactive current or residual voltage facilitates accurate, quick determination of current and conduction state of the iontophoresis apparatus, thereby facilitating the prevention of abnormal conditions.

In contrast, there is no disclosure in the Avrahami reference that relates to iontophoresis. That is, there is no disclosure in Avrahami of a detection circuit for a reactive current, nor is there any disclosure of a detection circuit for a residual voltage. For these reasons, it is respectfully submitted that the apparatus and methods disclosed in the Avrahami reference do not achieve the effects of the present invention. Consequently, it is believed that the Avrahami reference in no way anticipates or renders

unpatentably obvious the subject matter now called for in the claims herein. Therefore, it is believed that the Examiner would be justified in no longer maintaining this rejection. Withdrawal of the rejection is accordingly respectfully requested.

In view of the foregoing, it is respectfully submitted that the application is now in condition for allowance, and early action and allowance thereof is accordingly respectfully requested. In the event there is any reason why the application cannot be allowed at the present time, it is respectfully requested that the Examiner contact the undersigned at the number listed below to resolve any problems.

Respectfully submitted

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Date: December 29, 2002

MARKED-UP VERSION OF AMENDED CLAIMS 1-7

Please substitute the following amended Claims 1-7 for the original Claims 1-7 as follows:

1. (Amended) A device for iontophoresis supplying a drug to transdermal or transmucosal tissues, comprising:

first means having a detection circuit for detecting a [capacitance stored in] reactive current flowing through the transdermal or the transmucosal and/or a detection circuit for detecting a residual voltage developed in the transdermal or the transmucosal; and second means for determining a conduction state of current into the transdermal or the transmucosal based on the output detected by the first means.

2. (Amended) The device for iontophoresis according to Claim 1, wherein the [first means is a] detection circuit for [a] detecting the [a] reactive current [flowing through the transdermal or the transmucosal] includes a resistor coupled to an output terminal, a switch for sending one of positive and negative waveforms of current from the resistor, and a capacitor for smoothing out the current waveform from the switch.

3. (Amended) The device for iontophoresis according to Claim 1, wherein the [first means is a] detection circuit for detecting [a] the residual voltage [developed in the transdermal or the transmucosal] includes a discharging resistor coupled between output terminals.

4. (Amended) A method for determining an operation of an

iontophoresis apparatus, wherein [a capacitance stored in] a reactive current flowing through the transdermal or the transmucosal and/or a residual voltage developed in the transdermal or the transmucosal is detected to determine a conduction state of current flowing into the transdermal or the transmucosal.

5. (Amended) The method for detecting an operation of an iontophoresis apparatus according to Claim 4, wherein the detection of the [capacitance] reactive current is carried out [by detecting a reactive current flowing through the transdermal or the transmucosal] so as to send one of positive and negative waveforms of current from a resistor coupled to an output terminal by using a switch and smoothing out the current waveform by using a capacitor.

6. (Amended) The method for detecting an operation of an iontophoresis apparatus according to Claim 4, wherein the detection of the [capacitance] residual voltage is carried out by [detecting a residual voltage developed in the transdermal or the transmucosal] using a discharging resistor coupled between output terminals.

7. (Amended) An iontophoresis apparatus comprising:

a preparation for iontophoresis, holding a drug; and a device for iontophoresis having means for generating an electrical output to supply a drug from the preparation into transdermal or transmucosal and means for detecting [a capacitance stored in the] a reactive current flowing through the transdermal or the

transmucosal and/or a residual voltage developed in the transdermal or the transmucosal to determine a conduction state of a current flowing into the transdermal or the transmucosal.

DOCKET NO. MUR-027-USA-PCT

CERTIFICATE OF MAILING

I hereby certify that this amendment, transmittal in duplicate, 3-month Petition For Extension of Time in duplicate and Verified English Translation of Japanese Patent Application 11-45696 filed February 24, 1999, in Docket No. MUR-027-USA-PCT, Serial No. 09/890,284, filed on August 13, 2001, is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to:

Assistant Commissioner for Patents
Washington, D.C 20231

on December 30, 2002

Donald E. Townsend